

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Itzhak Bentwich

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Art Unit: 1635

Examiner: VIVLEMORE, TRACY ANN

Title: BIOINFORMATIALLY DETECTABLE  
GROUP OF NOVEL VIRAL  
REGULATORY GENES AND USES  
THEREOF**AMENDMENT AND SUPPLEMENTAL REPLY UNDER 37 C.F.R. § 1.111(a)(2)**

Dear Sir:

In response to the Office Action mailed November 14, 2006 (the "Office Action"), and supplemental to the reply filed April 16, 2007, please consider the remarks below in accordance with the Rule of Practice.

Submitted herewith is the requisite fee of \$360.00 under 37 C.F.R. § 1.16(j) for multiple dependent claims. No other fees are believed to be due in connection with the filing of this paper, however, should any fees be deemed necessary, the Commissioner is hereby authorized to deduct any such fees from Deposit Account No. 50-1662 referencing the above docket number.

**Amendments to the Claims** begin at page 2 of this response; and **Remarks** begin at page 4.

## AMENDMENTS TO THE CLAIMS

1. -20. (Canceled)

21. (Currently Amended) An isolated nucleic acid consisting of ~~18 to 120~~ X nucleotides wherein the sequence of the nucleic acid comprises:

- (a) ~~at least 18~~ Y consecutive nucleotides of SEQ ID NO: ~~46759-4641~~ or 4642;
- (b) an RNA equivalent of (a);
- (c) a sequence at least ~~34/58~~ 62.5% identical to (a) or (b); or
- (d) the complement of any one of (a)-(c),

wherein

X = 18 to 24,

Y ≥ 18, and

X ≥ Y.

22. - 40 (Canceled)

41. (New) The nucleic acid of claim 21, wherein the sequence of (c) is at least 70.8% identical to (a) or (b).

42. (New) The nucleic acid of claim 21, wherein the sequence of (c) is at least 79.2% identical to (a) or (b).

43. (New) The nucleic acid of claim 21, 41, or 42, wherein X = Y.

44. (New) A vector comprising the nucleic acid according to claim 21, 41, or 42.

45. (New) A vector comprising the nucleic acid of claim 43.

46. (New) An isolated nucleic acid consisting of X nucleotides wherein the sequence of the nucleic acid comprises:

- (a) Y consecutive nucleotides of SEQ ID NO: 4641 or 4642;
- (b) an RNA equivalent of (a);
- (c) a sequence at least 62.5% identical to (a) or (b); or
- (d) the complement of any one of (a)-(c)

wherein

X = 50 to 120,

Y ≥ 18,

X ≥ Y.

47. (New) The nucleic acid of claim 46, wherein the sequence of (c) is at least 70.8% identical to (a) or (b).

48. (New) The nucleic acid of claim 46, wherein the sequence of (c) is at least 79.2% identical to (a) or (b).

49. (New) A vector comprising the nucleic acid according to claim 46, 47, or 48.

## REMARKS

### 1. Preliminary Remarks

#### a. Status of the Claims

Claims 21-40 are pending this application. Claim 21 is amended, and claims 41-49 are new. In order to expedite prosecution and without prejudice to seeking claims of similar scope in a continuing application, claims 22-40 are hereby canceled. Upon entry of these amendments, claims 21, and 41-49 are pending and at issue. Applicant respectfully requests entry of the foregoing amendments and following remarks.

#### b. Interview Summary

The undersigned would like to thank Examiner Vivemore and Examiner Zara for the courtesy of the interview of May 8, 2007 during which the cited art and the reply filed April 16, 2007 were discussed. This Supplemental Reply is filed to address the issues raised by the Examiner, and is believed to place the application in condition for allowance.

#### c. Amendments to the Claims

Previous claim 21 recited SEQ ID NO: 46759, which is a polycistronic precursor comprising the hairpins set forth in SEQ ID NOS: 1916 and 1917, and the miRNAs set forth in SEQ ID NOS: 4641 and 4642. For the convenience of the Examiner, Appendix A shows the relationship of the polycistronic precursor and related sequences.

Amended claim 21 now recites the miRNAs sequences set forth in SEQ ID NOS: 4641 and 4642. The length of the nucleic acid of amended claim 21 is X nucleotides, wherein  $X \geq 18$  to 24. Support for this length can be found at paragraph 0014 of the specification as originally filed. Paragraph 0014 recites, "RNA encoded by the bioinformatically detectable novel viral gene is about 18 to about 24 nucleotides in length..."

Part (a) of claim 21 is also amended to recite that the sequence of the nucleic acid may comprise a sequence with Y consecutive nucleotides of SEQ ID NOS: 4641 or 4642, wherein  $Y \geq 18$  and  $X \geq Y$ . Support for part (a) of claim 21 can be found at paragraph 0014 as described above.

Claim 21, limitation (c) is amended to recite that the sequence of the nucleic acid comprises a sequence at least 62.5% identical to (a) or (b), support for which can be found at Figures 1930D/1 and 1931D/1, as originally filed. Figure 1930D/1 shows that 15 out of 24

(62.5%) nucleotides of the miRNA related to SEQ ID NO: 4641 are sufficient to target the binding site of LOC146229 as follows:

			TGC	GC		
<b>LOC146229</b>	5'	TAGGCAAT	GT	CTAGA	3'	SEQ ID:4641
<b>BINDING SITE1</b>	3'	ATCTGTTA	TA	GATCT	5'	SEQ ID:38117
			TAC	A-		

Figure 1931D/1 shows that 15 out of 24 (62.5%) nucleotides of the miRNA related to SEQ ID NO: 4642 likewise are sufficient to target the binding site of COL6A1 as follows:

			CT-	CACTAT		
<b>COL6A1</b>	5'	TAGCACCG	ATC	GTCT	3'	SEQ ID:4642
<b>BINDING SITE1</b>	3'	ATCGTGGC	TAG	CAGA	5'	SEQ ID:7584
			AAT	AGCTCC		

New claim 41 recites the nucleic acid of claim 21, wherein the sequence of (c) is at least 70.8% identical to (a) or (b), support for which can be found at Figure 1930D/1 and 1931D/1 as originally filed. Figure 1930D/1 shows that 17 out of 24 (70.8%) nucleotides of the miRNA related to SEQ ID NO: 4641 are sufficient to target the binding site of SNPH as follows:

			T	G	CCTA	A	
<b>SNPH</b>	5'	TAGGCAAT	GC	TG	GA	CAT	3'
<b>BINDING SITE1</b>	3'	ATCCGTTA	CG	AC	CT	GTA	5'
			C	-	AAC-	C	

Figure 1931D/1 shows that 17 out of 24 (70.8%) nucleotides of the miRNA related to SEQ ID NO: 4642 are sufficient to target the binding site of ZNF212 as follows:

			CTA	ACTA	-	
<b>ZNF212</b>	5'	TAGCACCG	TCC	TG	TCTC	3'
<b>BINDING SITE1</b>	3'	ATCGTGGC	AGG	AC	AGAG	5'
			AC-	GG-	G	

New claim 42 recites the nucleic acid of claim 21, wherein the sequence of (c) is at least 79.2% identical to (a) or (b), support for which can be found at Figure 1930D/1 and 1931D/1 as originally filed. Figure 1930D/1 shows that 19 out of 24 (79.2%) nucleotides of the miRNA related to SEQ ID NO: 4641 are sufficient to target the binding site of LOC151201 as follows:

			---	T	C	
<b>LOC151201</b>	5'	TAGGCAATT	GCG	GC	TAGAA	3'
<b>BINDING SITE1</b>	3'	ATCTGTAA	TGT	CG	ATCTT	5'
			TTC	-	A	

Figure 1931D/1 shows that 19 out of 24 (79.2%) of the nucleotides of the miRNA related to SEQ ID NO: 4642 are sufficient to target the binding site of KIAA1622 as follows:

		C - A CAC	
KIAA1622	5'	TAGCA C GCT TC	TATGTCTC 3' SEQ ID:4642
BINDING SITE1	3'	ATTGT G CGA AG	ATACAGAG 5' SEQ ID:27766
		A T C TA-	

New claim 43 is related to a nucleic acid consisting of 18 to 24 consecutive nucleotides of SEQ ID NO: 4641 or 4642, an RNA equivalent thereof, a sequence at least 62.5%, 70.8%, or 79.2% thereto, or the complement thereof. New claim 43 recites the nucleic acid of claims 21, 41, or 42, wherein X=Y, antecedent basis and support for which can be found as described above for amended claim 21.

New claim 44 recites a vector comprising the nucleic acid according to claim 21, 41, or 42, support for which can be found at paragraph 0023 of the specification as originally filed.

New claim 45 recites a vector comprising the nucleic acid of claim 43, support for which can be found as described above for new claim 44.

New claim 46 recites the hairpin sequences set forth in SEQ ID NOS: 4641 and 4642. The length of these hairpin-related nucleic acids is x nucleotides, wherein X= 50 to 120. Support for this length can be found at paragraph 0014 of the specification as originally filed. Paragraph 0014 recites in part, "RNA precursor is about 50 to about 120 nucleotides in length..." New claim 46 also recites that the sequence of the nucleic acid comprise Y consecutive nucleotides of SEQ ID NO: 4641 or 4642, wherein  $Y \geq 18$  and  $X \geq Y$ , support for which can be found as described above for amended claim 21.

New claim 46, limitation (b) recites that the sequence of the nucleic acid comprises an RNA equivalent of limitation (a), support for which can be found at paragraph 0014 of the specification as originally filed.

New claim 46, limitation (c) recites that the sequence of the nucleic acid is a sequence at least 62.5% identical to (a) or (b), support for which can be found as described above for amended claim 21.

New claim 46, limitation (d) recites that the sequence of the nucleic acid may be the complement of any one of (a)-(c), support for which can be found at paragraphs 0015 and 0016 of the specification as originally filed. Paragraphs 0015 and 0016 recite in part:

...further provided in accordance with another preferred embodiment of the present invention a method for anti-viral treatment comprising neutralizing said RNA ... the neutralizing comprises: synthesizing a complementary nucleic acid molecule...

New claim 47 recites the nucleic acid of claim 46, wherein the sequence of (c) is at least 70.8% identical to (a) or (b), support for which can be found as described above for new claim 41.

New claim 48 recites the nucleic acid of claim 46, wherein the sequence of (c) is at least 79.2% identical to (a) or (b), support for which can be found as described above for new claim 42.

New claim 50 recites a vector comprising the nucleic acid according to claim 46, 47, or 48, support for which can be found at paragraph 0023 of the specification as originally filed.

## **2. Patentability Remarks**

### **a. 35 U.S.C. §102**

#### **(1) Rejection Pursuant to 35 U.S.C. § 102(b)**

##### ***Claims 21, 24, and 37***

On page 11 of the Office Action, the Examiner rejects claims 21, 24 and 37 under 35 U.S.C. § 102(b) as allegedly being anticipated by Dean et al, U.S. Patent No. 6,136,603 ("Dean"). Applicant respectfully disagrees.

Appendix A shows that the Dean sequence aligns to a region between the hairpin sequences of SEQ ID NOS: 1916 and 1917. As amended, the claims are related to the hairpin nucleic acid sequences set forth in SEQ ID NOS: 1916 and 1917, and the miRNA sequences set forth in SEQ ID NOS: 4641 and 4642. As shown in Appendix A, the claimed sequences do not overlap with the sequence of Dean. Accordingly, Dean fails to teach or suggest the claimed sequences. In view of the foregoing amendments and remarks, Applicant respectfully requests that the rejection under 35 U.S.C. § 102(b) be withdrawn.

#### **(2) Rejection Pursuant to 35 U.S.C. § 102(e)**

##### ***Claims 21, 35, 37, and 39***

On page 12 of the Office Action, the Examiner rejects claims 21, 35, 37, and 39 under 35 U.S.C. § 102(e) as allegedly being anticipated by Homburger et al, U.S. Patent No. 6,703,491 ("Homburger"). Applicant respectfully disagrees.

Appendix A shows that the Homburger sequence aligns to a region between the hairpin sequence of SEQ ID NOS: 1916 and 1917. As amended, the claims are related to the hairpin nucleic acid sequences set forth in SEQ ID NOS: 1916 and 1917, and the miRNA sequences set forth in SEQ ID NOS: 4641 and 4642. As shown in Appendix A, the claimed sequences do not overlap with the sequence of Homburger. Accordingly, Dean fails to teach or suggest the claimed sequences. In view of the foregoing amendment and remarks, Applicant respectfully submits that the rejection under 35 U.S.C. 102(b) be withdrawn.

***Claims 21 and 37***

On page 13 of the Office Action, the Examiner rejects claims 21 and 37 under 35 U.S.C. § 102(e) as allegedly being anticipated by Okamoto et al, U.S. Patent No. 6,849,431 (“Okamoto”). Applicant respectfully disagrees.

Appendix A shows that the Okamoto sequence aligns to a region between the hairpin sequence of SEQ ID NOS: 1916 and 1917. As amended, the claims are related to the hairpin nucleic acid sequences set forth in SEQ ID NOS: 1916 and 1917, and the miRNA sequences set forth in SEQ ID NOS: 4641 and 4642. As shown in Appendix A, the claimed sequences do not overlap with the sequence of Okamoto. Accordingly, Okamoto fails to teach or suggest the claimed sequences. In view of the foregoing amendment and remarks, Applicant respectfully submits that the rejection under 35 U.S.C. 102(e) be withdrawn.

**b. 35 U.S.C. §103(a)**

**(1) Rejection Pursuant to 35 U.S.C. § 103(a)**

***Claims 21, 24, 35, 37, and 39***

On page 14 of the Office Action, the Examiner rejects claims 21, 24, 35, 37, and 39 under 35 U.S.C. § 103(a) as allegedly being obvious over Dean in view of Noonberg et al, U.S. Patent No. 5,624,803 (“Noonberg”). Applicant respectfully disagrees.

In order to establish obviousness, the cited prior art references must teach or suggest all the claim limitations. *See* M.P.E.P. 2143. As shown in Appendix A and described above, the claimed sequences do not overlap with the sequence of Dean. Accordingly, Dean fails to teach or suggest the claimed sequence. Furthermore, Noonberg does nothing to correct the deficiency of Dean because Noonberg only teaches a means for inserting vectors via liposomes or localized injection.



In conclusion, Applicant submits that Dean either alone or in combination with Noonberg neither teaches nor suggests the claimed subject matter of new claims 41-48. Accordingly, without such teaching or suggestion, a *prima facie* case of obviousness has not been made for new claims 41-48. In view of the foregoing remarks and amendments, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

### 3. Conclusion

Applicant respectfully submits that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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Dated: May 17, 2007

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